

What is claimed is:

1. A pharmaceutical composition useful for topical treatment of an anal disease, said composition comprising an organic nitric oxide donor in combination with a carrier, in a form selected from the group consisting of a powder, an aerosol, a liquid to include a thickened liquid, an ointment and a suppository; wherein if the organic nitric oxide donor is only nitroglycerin and the composition is a soft paraffin or petroleum based ointment then the nitroglycerin is present in an amount excluding 2.0% by weight.

2. The composition of claim 1, wherein the organic nitric oxide donor is nitroglycerin.

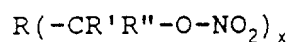
3. The composition of claim 2, which is an ointment.

4. The composition of claim 1, wherein nitroglycerin is the organic nitric oxide donor, present in an amount from about 0.25 to about 0.45 percent by weight, in an ointment.

5. The composition of claim 1, wherein nitroglycerin is the organic nitric oxide donor, present in an amount from about 0.07 to about 0.15 percent by weight, in an ointment.

6. The composition of claim 1, which is a suppository.

7. The composition of claim 1, wherein the organic nitric oxide donor includes at least one organic nitrate represented by the following general formula:



wherein:

R, R' and R'' are, independently at each occurrence, organic or hydro moiety or covalent bond, and x is an integer from 1 to about 12.

8. The composition of claim 7, wherein R is a 2 to about 12 carbon hydrocarbon or oxygen-substituted hydrocarbon;

R' is of 2 to 6 carbons and from 0 to 2 oxygen(s), a hydro moiety or a covalent bond;

R'' is a hydro moiety; and

x is from 2 to 6.

9. The composition of claim 8, which excludes nitroglycerin; ethylene glycol dinitrate; isopropyl nitrate; glyceryl-1-mononitrate; glyceryl-1,2-dinitrate; glyceryl-1,3-dinitrate; butane-1,2,4-triol-trinitrate; erythrityl tetranitrate; pentaerythrityl tetranitrate; isosorbide mononitrate; and isosorbide dinitrate.

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10. The composition of claim 1, wherein the organic nitric oxide donor includes at least one organic nitrate selected from the group consisting of ethylene glycol dinitrate; isopropyl nitrate; glyceryl-1-mononitrate; glyceryl-1,2-dinitrate; glyceryl-1,3-dinitrate; butane-1,2,4-triol-trinitrate; erythrityl tetranitrate; pentaerythrityl tetranitrate; isosorbide mononitrate; and isosorbide dinitrate, in an ointment or suppository form.

11. The composition of claim 1, wherein the organic nitrate donor is selected from the group consisting of one or more of erythrityl tetranitrate; pentaerythrityl tetranitrate; and isosorbide dinitrate.

12. A pharmaceutical composition useful for treating anal disease comprising an organic nitric oxide donor in combination with a corticosteroid and a pharmaceutically acceptable topical carrier.

13. The composition of claim 12, wherein the organic nitric oxide donor is nitroglycerin.

14. The composition of claim 13, wherein the corticosteroid is hydrocortisone.

15. The composition of claim 12, wherein a topical anesthetic is also present.

16. A pharmaceutical composition useful for treating anal disease comprising an organic nitric oxide donor in combination with a topical anesthetic and a carrier.

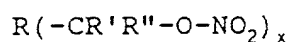
17. The composition of claim 16, wherein the organic nitric oxide donor is nitroglycerin.

18. The composition of claim 17, wherein the topical anesthetic is dibucaine.

19. A method for treating an anal disease comprising contacting an appropriate anal area with an effective amount of nitric oxide.

20. The method of claim 19, wherein the nitric oxide is delivered by release from an organic nitric oxide donor.

21. The method of claim 20, wherein the organic nitric oxide donor is an organic nitrate represented by the following general formula:



wherein:

R, R' and R'' are, independently at each occurrence organic or hydro moiety or covalent bond, and x is an integer from 1 to about 12.

22. The method of claim 21, wherein R is a 2 to about 12 carbon hydrocarbon or oxygen-substituted hydrocarbon;

R' is of 2 to 6 carbons and from 0 to 2 oxygen(s), a hydro moiety or a covalent bond;

R'' is a hydro moiety; and

x is from 2 to 6.

23. The method of claim 20, wherein the organic nitric oxide donor is nitroglycerin.

24. The method of claim 20, wherein at least one agent selected from the group consisting of a corticosteroid and a topical anesthetic is employed in conjunction with the nitric oxide donor.

25. The method of claim 21, wherein at least one agent selected from the group consisting of a corticosteroid and a topical anesthetic is employed in conjunction with the nitric oxide donor.

26. The method of claim 25, wherein the corticosteroid is hydrocortisone, and the topical anesthetic is dibucaine.

27. The method of claim 19, wherein anal pain is controlled thereby.

28. The method of claim 19, wherein the anal disease is anal fissure or ulcer.

29. The method of claim 19, wherein the anal disease is hemorrhoid disease.

30. The method of claim 19, wherein the anal disease is levator spasm.

31. The method of claim 28, wherein nitroglycerin is employed.

32. The method of claim 29, wherein nitroglycerin is employed.

33. The method of claim 30, wherein nitroglycerin is employed.

34. The method of claim 31, wherein anal pain is controlled thereby.

35. The method of claim 32, wherein anal pain is controlled thereby.

36. The method of claim 33, wherein anal pain is controlled thereby.

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Abstract of the Disclosure

A pharmaceutical composition contains a nitric oxide donor and advantageously an optional corticosteroid and/or topical anesthetic. The composition is useful in a method for treating anal disorders such as anal fissure, anal ulcer, hemorrhoidal disease, levator spasm, and so forth, by topical application to or proximate the affected area.

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Stephen R. Gorfine)

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Attorney Docket No. GRFS.54767

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NITRIC OXIDE DONOR COMPOSITION)

AND METHOD FOR TREATMENT OF)

ANAL DISORDERS)

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington DC 20231

Dear Sir:

Prior to examination, please amend the above-identified application as follows:

In the Title

Please delete "AND METHOD".

In the Claims

Please amend the claims as follows:

Cancel claim 1.

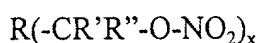
Please add the following claims:

--37. In an applicator, an amount of a pharmaceutical composition effective for topical treatment of an anal disease, said composition comprising an organic nitric oxide donor in combination with a carrier.

38. The composition of claim 37, wherein the organic nitric oxide donor is present in the composition in an amount from about 0.01 to about 10 percent by weight.

39. The composition of claim 37, wherein the organic nitric oxide donor is present in the composition in an amount from about 0.01 to about 10 percent by weight.

40. The composition of claim 37, wherein the organic nitric oxide donor is an organic nitrate represented by the following general formula:



wherein:

R, R' and R'' are, independently at each occurrence, organic or hydro moiety or covalent bond, and

x is an integer from 1 to about 12.

41. The composition of claim 40, wherein

R is a 2 to about 12 carbon hydrocarbon or oxygen-substituted hydrocarbon;

R' is of 2 to 6 carbons and from 0 to 2 oxygen(s), a hydro moiety or a covalent bond;

R'' is a hydro moiety; and

x is from 2 to 6.

42. The composition of claim 37, wherein the organic nitric oxide donor comprises one or more of ethylene glycol dinitrate, isopropyl nitrate, glyceryl-1-mononitrate, glyceryl-1,2-dinitrate, glyceryl-1,3-dinitrate, nitroglycerin, butane-1,2,4-triol-trinitrate, erythrityl tetranitrate, pentaerythrityl tetranitrate, isosorbide mononitrate, and isosorbide dinitrate.

43. The composition of claim 37, wherein the organic nitric oxide donor comprises nitroglycerin.

44. The composition of claim 43, wherein the nitroglycerin is present in the composition in an amount of from about 0.01 to about 5% by weight.

45. The composition of claim 37, wherein the organic nitric oxide donor comprises isosorbide dinitrate.

46. The composition of claim 45, wherein the isosorbide dinitrate is present in the composition in an amount of from about 0.01 to about 7.5% by weight.

47. The composition of claim 37, wherein the organic nitric oxide donor comprises erythrityl tetranitrate.

48. The composition of claim 47, wherein the erythrityl tetranitrate is present in the composition in an amount of from about 0.01 to about 4% by weight.

49. The composition of claim 37, wherein the organic nitric oxide donor comprises pentaerythrityl tetranitrate.

50. The composition of claim 49, wherein the pentaerythrityl tetranitrate is present in the composition in an amount of from about 0.01 to about 4% by weight.

51. The composition of claim 37, including at least one agent selected from the group consisting of a corticosteroid and a topical anesthetic in the composition.

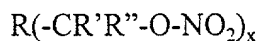
52. The composition of claim 37, wherein said amount of the pharmaceutical composition is effective to control pain associated with said anal disease.

53. A pharmaceutical composition in a suppository form and effective for topical treatment of an anal disease, said composition comprising an organic nitric oxide donor in combination with a carrier.

54. The composition of claim 53, wherein the organic nitric oxide donor is present in the composition in an amount from about 0.01 to about 10 percent by weight.

55. The composition of claim 53, wherein the organic nitric oxide donor is present in the composition in an amount from about 0.01 to about 10 percent by weight.

56. The composition of claim 53, wherein the organic nitric oxide donor is an organic nitrate represented by the following general formula:



wherein:

R, R' and R'' are, independently at each occurrence, organic or hydro moiety or covalent bond, and

x is an integer from 1 to about 12.

57. The composition of claim 56, wherein

R is a 2 to about 12 carbon hydrocarbon or oxygen-substituted hydrocarbon;

R' is of 2 to 6 carbons and from 0 to 2 oxygen(s), a hydro moiety or a covalent bond;

R'' is a hydro moiety; and

x is from 2 to 6.

58. The composition of claim 53, wherein the organic nitric oxide donor comprises one or more of ethylene glycol dinitrate, isopropyl nitrate, glyceryl-1-mononitrate,

glyceryl-1,2-dinitrate, glyceryl-1,3-dinitrate, nitroglycerin, butane-1,2,4-triol-trinitrate, erythrityl tetranitrate, pentaerythrityl tetranitrate, isosorbide mononitrate, and isosorbide dinitrate.

59. The composition of claim 53, wherein the organic nitric oxide donor comprises nitroglycerin.

60. The composition of claim 59, wherein the nitroglycerin is present in the composition in an amount of from about 0.01 to about 5% by weight.

61. The composition of claim 53, wherein the organic nitric oxide donor comprises isosorbide dinitrate.

62. The composition of claim 61, wherein the isosorbide dinitrate is present in the composition in an amount of from about 0.01 to about 7.5% by weight.

63. The composition of claim 53, wherein the organic nitric oxide donor comprises erythrityl tetranitrate.

64. The composition of claim 63, wherein the erythrityl tetranitrate is present in the composition in an amount of from about 0.01 to about 4% by weight.

65. The composition of claim 53, wherein the organic nitric oxide donor comprises pentaerythrityl tetranitrate.

66. The composition of claim 65, wherein the pentaerythrityl tetranitrate is present in the composition in an amount of from about 0.01 to about 4% by weight.

67. The composition of claim 53, including at least one agent selected from the group consisting of a corticosteroid and a topical anesthetic in the composition.

68. The composition of claim 53, wherein said amount of the pharmaceutical composition is effective to control pain associated with said anal disease.--